Claims

- Method for culturing cells in order to produce substances characterized in that,

 a cell producing substances is cultured under glucose limitation (DGL),
 wherein the DGL (DGL = qGlc/qGlc_{max} where qGlc = observed current specific glucose consumption rate and qGlc_{max} = maximum known specific glucose consumption rate for these cells) is larger than the DGL which only leads to the maintenance (DGL_{maintenance}) of the cell and is ≤ 0.5, wherein DGL_{maintenance} = qGlc_{maintenance}/qGlc_{max} where qGlc_{maintenance} = the observed specific glucose consumption rate for pure maintenance metabolism and qGlc_{max} = maximum known specific glucose consumption rate for these cells.
- 2. Method as claimed in claim 1, characterized in that the DGL is ≤ 0.4 or ≤ 0.3 .
- 3. Method as claimed in claim 1 or 2, characterized in that the amount of fed glucose is not more than 50 % of that which can be maximally consumed by the maximum expected cell count without glucose limitation.
- 4. Method as claimed in claim 3, characterized in that the amount of fed glucose is not more than 35 % of that which can be maximally consumed by the maximum expected cell count without glucose limitation.

- 5. Method as claimed in one of the claims 1 to 4, characterized in that one component is used from the group of cell lines comprising CHO such as CHO-K1, BHK such as BHK-21, hybridoma, myeloma cells such as NS/O, other mammalian cells and insect cells or other higher cells.
- Method as claimed in one of the claims 1 to 5, characterized in that the produced substances are proteins or polypeptides.
- 7. Method as claimed in claim 6, characterized in that the produced substances are fusion proteins, MUC1-IgG2a, MUC2-GFP-Cterm, EPO, interferons, cytokines, growth factors, hormones, PA, immuno-globulins, fragments of immunoglobulins or other glycoproteins.
- 8. Method as claimed in one of the claims 1 to 7, characterized in that a glucose-containing medium is used which is not limiting with regard to other nutrient components before glucose limitation occurs.
- Method as claimed in claim 8,
 characterized in that
 the glucose is fed separately from other substrates.
- Method as claimed in one of the claims 1 to 9, characterized in thatit is carried out in a pH range of 6.7 7.7.

- 11. Method as claimed in one of the claims 1 to 10, characterized in that it is carried out in a temperature range in which irreversible destruction of the product does not occur.
- Method as claimed in one of the claims 1 to 11,characterized in thatit is operated in a continuous process with at least partial cell retention.
- 13. Method as claimed in one of the claims 1 to 12, characterized in that it is carried out in a fed-batch process.
- 14. Method as claimed in one of the claims 1 to 13,characterized in thatit is started as a batch and continued as a fed-batch or continuous process.
- 15. Method as claimed in one of the claims 1 to 14,characterized in thatit is carried out with cells whose production is not coupled to growth.